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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/578,561	03/01/2007	Howard J. Federoff	176/62732 (6-I275)	7894

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EXAMINER	
KELLY, ROBERT M	

ART UNIT	PAPER NUMBER
1633	

MAIL DATE	DELIVERY MODE
02/23/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/578,561	FEDEROFF ET AL.	
	Examiner	Art Unit	
	ROBERT M. KELLY	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 July 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-31,33,34 and 49-51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-31,33,34 and 49-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *See Continuation Sheet*.

Continuation of Attachment(s) 6). Other: http://www.everythingbio.com/glos/definition.php?word=accessory+protein and In re Alonso 88 USPQ 1849 (Fed Cir 2008)

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DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/6/10 has been entered.

Claims 28 and 50 are presently amended.

Claim 51 is newly presented.

Claims 28-31, 33, 34, and 49-51 are presently pending.

Specification

The amendment filed 10/28/09 remains objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: the removal of what Applicant considered to be the essential HSV genes opens up the possible scope to that scope which may exist in the future, and hence, is new matter.

Applicant is required to cancel the new matter in the reply to this Office Action.

Response to objection to Specification for new matter

Applicant's response of 7/6/10 has been fully considered but is not found persuasive.

Applicant argues that Roizman elucidates what was considered the essential genes of HSV-1 in cell culture, and the MPEP states that information which is well known in the Art need not be described, and therefore, although there was an error in citing figure 3 as a list of essential genes, the Artisan would readily understand which genes are essential (pp. 4-5).

Such is not persuasive. Applicant's disclosure also describes the internet site at Los Alamos Labs for a report of essential HSV-1 genes (p. 24, paragraph 1, of the original disclosure). As the Examiner has stated, such is subject to change as the technology develops, and hence, there appears to be a guidance to look to the future. The Examiner will accept an amendment to bring in the listing of essential genes described by Roizman as the essential genes, and not object, as clearly the specificaiton refers to Roizman's disclosures for such. However, Applicant should very carefully disclose where and which genes are listed in each of Roizman's documents to make sure that they are adequately provided, and not subject to further objection. To wit, if Roizman's documents do not describe the exact same genes, the Examiner has to clearly see how the Artisan would have arrived at the same genes as Applicant lists.

Claim Rejections - 35 USC § 112 - enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 28-31, 33, 34, and 49-51 remain and/or are newly rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for reasons of record.

Claims 28, 50, and 51 contains a limitation to "encode all essential HSV genes". The specification as originally filed teaches that the genes in Figure 3 are those that are known to be "essential", but the present amendment to the specification removes such a statement, and relies only upon the Los Alamos National Laboratory internet site, which can change as technology develops. Hence, it is not clear which genes are meant to be encompassed by such limitation due to the amendments.

Claims 29-31, 33, 34, and 49 are rejected for the same basis as Claim 28, because they depend and do not overcome the lack of clarity.

Response to Argument – clarity

Applicant's argument of 7/6/10 refers to the arguments of the specification, but as seen above, such is not persuasive. Applicant must rectify the situation properly to avoid future-considered-essential genes.

Claim Rejections - 35 USC § 112 – new matter

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 28-31, 33, 34, and 49-51 remain and/or are newly rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, for comprising new matter, for reasons of record. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification has been amended to remove the listing of essential HSV genes, as the present amendment to the paragraph at page 23, line 25, indicates.

However, the claims require "encode all essential HSV genes".

By removing the limitation as to what Applicant regards as essential HSV genes at the time of invention, Applicant has introduced new matter, because the knowledge in the Art changes over time, and hence, what was regarded by Applicant to be essential are not necessarily those that are regarded as essential in the future.

Therefore, the claims are properly rejected for comprising new matter.

Response to Argument – new matter

Applicant's argument of 7/6/10 refers to the arguments of the specification, but as seen above, such is not persuasive. Applicant must rectify the situation properly to avoid future-considered-essential genes.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 28-31, 33, 34 and 49 are newly rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 28-31, 33, 34, and 49 encompass a generic accessory protein. The specification provides no description of even one example as being an "accessory protein", but simply generic references to an accessory protein (e.g., paragraphs 21-22), and it is noted that TtxFC and KLH are noted to be molecular adjuvants, and not accessory proteins (e.g., paragraph 22).

However, it is also noted there exists description for VHS protein (e.g., paragraph 56), which, although not specifically stated to be an accessory protein, does appear to be an accessory protein, as it helps with the relatively-increased formation of viral proteins (e.g., paragraphs 56-57). Applicant should note the definition of "accessory protein" provided in the attached appendix (http://www.everythingbio.com/glos/definition.php?word=accessory+protein).

However, Applicant has provided no other description of another "accessory protein" in the specification. In fact, it is almost hard to deduce that VHS is an accessory protein, but the Examiner cannot imagine what else Applicant meant besides VHS protein.

Further, In re Alonso 88 USPQ 1849 (Fed Cir 2008) makes clear that a single embodiment does not demonstrate possession of a genera.

Therefore, the Artisan would not have understood Applicant to have been in possession of the invention as claimed at the time of filing.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 28-31, 33, 34, 49, and 50 remain rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,972,127 to Schenk; U.S. Patent No. 6,972,127 to Schenk; U.S. Patent No. 6,946,135 to Schenk; Stavropoulos, et al. (1998) Journal of Virology, 72(9):7137-43; Saeki, et al. (1998) Human Gene Therapy, 9: 2787-94, and as further evidenced by Town, et al. (2002) Journal of Neuroimmunology, 132: 49-59, for reasons of record.

Schenk '855 claims methods of treating diseases with Abeta deposits, including Alzheimer's disease, by administration of Abeta to thereby raise antibodies and treating the disease by the antibodies raised (Claims). Schenk '127 claims similar treatments, and teaches in the specification that the peptide may be alternatively delivered via a viral vaccine, wherein the protein is encoded in a vector, which is expressed by the cells, and in one embodiment HSV may be used as the vector, which should be non-pathogenic or attenuated (e.g., Section entitled "III. Therapeutic Agents", subsection entitled "1. Alzheimer's Disease", paragraph 9). Schenk '135 Claims treatment of the same with Abeta linked to a carrier molecule, and teaches in the specification that Keyhole limpet hemocyanin and tetanus toxoid may be used (Section entitled "III. Therapeutic Agents", subsection "1. Alzheimer's Disease", subsection entitled "3. Carrier Proteins").

Stavropoulos and Saeki both discuss the growth of amplicons in the absence of helper virus. Stavropoulos discusses the second-generation packaging system for HSV amplicons, which is centered on the use of five overlapping HSV-1 cosmid clones that together encode the wild-type viral genome but lack the required sequences for cleavage and packaging (p. 7138, col. 1, paragraph 2). Stavropoulos then modified the system by providing a single BAC with all the elements required for replication and packaging of the amplicon, but lacking the viral sequences

for cleavage and packaging (e.g., p. 7140, col. 2, paragraph 2-p. 7141, col. 1, paragraph 2). Saeki teaches similar prior art knowledge with regard to the five overlapping HSV-1 cosmid clones for production of helper-free virus amplicons (e.g., p. 2788, paragraph bridging columns) and similar production of a single bacterial artificial chromosome for production of helper-free viral amplicons (p. 2788, col. 2, paragraph 2). Still further, both Stavropoulos and Saeki teach that the amplicons contain nucleic acid sequences encoding an accessory protein for replication in E. coli (e.g., Saeki, p. 2787, paragraph bridging columns, reciting the use of antibiotic resistance gene for amplicillin).

With regard to inducing a Th2 mediated immune response, Abeta has been shown by Town to so-induce such a response (e.g., Title), and, absent reason to believe otherwise, the desired effect is there, because any absence of comment does not mean the structure is the same.

With regard to the presence of a nucleic acid encoding VHS, at least Saeki has nothing that indicates that such gene has been removed, and hence, absent reason to believe otherwise, the nucleic acid may be present in the helper-free virus systems.

Lastly, one may question whether a nucleic acid could provide protein for inducing immune response to the Abeta protein. However, as is shown in Herrlinger, vaccination therapy works, and hence, protein is produced in high enough levels to have an affect (whole article, and discussing previous findings (p.1436).

Hence, it would have been obvious to modify the HSV vectors of Schenk to deliver a gene encoding Abeta and a gene encoding keyhole limpet hemocyanin, and grow such in a helper-free virus method like that of Stavropoulos and Saeki, to then administer the helper-free viral amplicon to treat Alzheimer's disease. The Artisan would do so to treat the disease.

Moreover, the Artisan would have a reasonable expectation of success, as Schenk teaches it will work, and claims similar protein therapy, Stavropoulos and Saeki teach the method of amplicon manufacture, and Herrlinger demonstrates the biologically-relevant levels of protein being produced.

Response to Argument - 103, Schenk (3), Stravopoulos, and Saeki (as by Towne)

Applicant's response has been fully considered but is not found persuasive.

Applicant argues that he co-transfecting step in amended claim 28 indicates that the vectors are unlinked, and therefore the claims are not obvious, because the accessory protein is encoded in the BAC (p. 7, paragraph 4).

Such is not persuasive. There are at least two elements which are transfected in the present case: the amplicon and the BAC. The question remains then, is the nucleic acid encoding an accessory protein limited to being a separate nucleic acid from (i) the amplicon plasmid, and (ii) the one or more vectors that, individually or collectively, encode all essential HSV genes, but exclude all cleavage/packaging signals? The answer to this, is no. There is no such requirement. In fact, the requirement appears to indicate that the nucleic acid, not being a "vector" would suggest that it can be within a vector. If anything, the language suggests it is part of the one or more vectors ... .

Applicant argues that Claim 52 is also non-obvious (pp. 7-8, paragraph bridging).

Such is not persuasive. There is no claim 52 of record in this case yet. For sake of completeness however, it is noted that Claim 50 may be the claim which is argued. The Argument is that HVS protein is not taught as an accessory protein. Such is not persuasive because the 5 overlapping cosmids of Saeki may be used, and further, there is no requirement for

the VHS to be expressed, but just encoded, and therefore, even Stravopolous will suffice for the rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 28-31, 33, 34, 49, and 50 remain, and Claim 51 is newly, rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,972,127 to Schenk; U.S. Patent No. 6,972,127 to Schenk; U.S. Patent No. 6,946,135 to Schenk; Stavropoulos, et al. (1998) Journal of Virology, 72(9):7137-43; Saeki, et al. (1998) Human Gene Therapy, 9: 2787-94, and as further evidenced by Town, et al. (2002) Journal of Neuroimmunology, 132: 49-59 as applied to claims 28-31, 33, 34, 49, and 50 above, and further in view of Whitley, et al. (1998) Clinical Infectious Diseases, 26: 541-53, for reasons of record, and as modified below.

This rejection is made to overcome possible arguments that VHS is actually deleted in the vector systems of Saeki.

While the art in the base rejection appears to make obvious the invention, there is no specific teaching that VHS is actually included in the Saeki vectors, and hence, where above, the Examiner has relied upon the inherent nature to state that absent reason to believe otherwise, here, the Examiner provides the knowledge that VHS may be used in such vector systems.

Whitley teaches VHS (A.K.A.: UL41) degrades all mRNA, but that because viral transcription occurs at a very high rate, viral protein synthesis is less affected than host cell protein synthesis (p. 543, col. 1, point 2).

Hence, the Artisan would be further motivated to include the VHS encoding sequence into the chromosome, or add it separately through another plasmid. The Artisan would do so to shut down host protein synthesis preferentially, and thereby increase the relative production of proteins for amplicon manufacture and packaging. Moreover, the Artisan would have a reasonable expectation of success, as Whitley teaches the known functional consequences of the VHS protein, and there is nothing to question the efficacy of the method.

Lastly, with regard to the provision of providing a cell expressing VHS protein, such is simply a design choice. The VHS may be provided as a vector separately transfected into the cell, but all that is required is the expression of VHS to affect the method, and as such, it may be integrated into the genome, or simply provided in another vector, prior to the other transfections, and still, the effect is logically the same. Hence, because it is utilized for an art-recognized purpose, it is reasonably predictable to effect production of HSV particles in the method. Therefore, it is also obvious.

Response to Argument – Further in view of Whitley

Applicant's argument of 7/6/10 has been fully considered but is not found persuasive.

Applicant argues that Whitley fails to teach or suggest that vhs would provide any affect on amplicon production or titer in helper-virus-free amplicon production, and that Stravopolous teaches its disruption (of expression) to eliminate its potentially toxic function to enhance

survival of the transduced cells, and therefore, it is argued that the combination of references teaches away from the invention (p. 8, paragraph 5).

Such is not persuasive. Stavopolous is concerned with the virus being toxic to the cells, but such is not a consideration, as Stavopolous is block it just to increase cell survival. However, Saeki's acknowledged 5-overlapping clone production method still has a vhs and still produces virus. Hence, the vhs does not inhibit viral production. Still further, the amplicon will still deliver the genes and produce protein, as the Saeki-recognized overlapping method still works to produce protein in cells subsequently transfected (Saeki teaches that the amplicons produced can transfect cells and express the heterologous transgene in Figure 3). If anything, Applicant is simply trying to get a patent for using a known-to-work method which is more dangerous than leaving out the transgene.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT M. KELLY whose telephone number is (571)272-0729. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Robert M Kelly/
Primary Examiner, Art Unit 1633